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Comparative Medicine Resources Directory

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Mutant Mouse Regional Resource Centers

The laboratory mouse has emerged as the primary mammalian system for genomics research and the preeminent surrogate model system for human disease and normative biology. Approximately 90 percent of human genes share homology to genes within the mouse genome. With this similarity to humans, the mouse model has contributed enormously to fundamental concepts in cancer biology, immunology, transplantation biology, genetics, infectious disease, and many other fields.

A rapidly evolving and increasingly sophisticated technology has developed for creating mouse models, but there is a need for making these models available to the scientific community in order for them to have maximum impact. In response to the increased number of genetically modified mice created and used by the biomedical research community, the NCRR sponsored the development of the Mutant Mouse Regional Resource Centers (MMRRCs).

The centers are funded under a Cooperative Agreements mechanism that involves development of animal model resources with substantial scientific and programmatic coordination between NCRR and the performing centers. The MMRRC network comprises an Informatics Coordinating Center and four regional mutant mouse distribution facilities or nodes capable of husbandry, cryopreservation; storing and reconstructing embryos; phenotypic characterization (structural and behavioral); genetic quality control; maintenance of a mouse resource database; and distribution of genetically modified mice to investigators and institutions throughout the medical research community. These nodes are located at Harlan Sprague Dawley, Inc./University of Missouri; Taconic Farms, Inc.; the University of California, Davis; and the University of North Carolina at Chapel Hill.

The MMRRC network accepts genetic mouse strains to its collection, and investigators who have created such models are encouraged to donate them to the network where they will then be provided upon request to other investigators who will use them in research of human health, disease and treatments.

Research Emphasis/Objectives

The MMRRC nodes have three basic objectives:

- provide a research component to generate new information that is relevant to the mutant mouse resource;
- serve the needs of investigators in a variety of research areas where research is sponsored by NIH categorical institutes; and
- make mutant mice available to investigators on a local, regional, and national basis.

The Informatics Coordinating Center (ICC) at The Jackson Laboratory provides an electronic network linking the MMRRCs by maintaining the database of the resources. The ICC database is updated continuously and includes live mouse and cryopreserved germplasm inventory from each MMRRC node.

Resources Provided/Submission of Strains

The MMRRC Web site provides application forms for submission of strain candidates to the MMRRC Program, information on standard supply levels and pricing of MMRRC strains, and the mechanism to request strains from the MMRRC nodes. The site can be reached at www.mmrrc.org.

Future MMRRC Grant Opportunities

NCRR anticipates expanding the MMRRC resources in the future. Further information about grant opportunities may be obtained from:

Division of Comparative Medicine
National Center for Research Resources
National Institutes of Health
One Democracy Plaza, Room 948
6701 Democracy Boulevard, MSC 4874
Bethesda, Maryland 20892-4874
Telephone: 301-435-0744
FAX: 301-480-3819
e-mail: CMADIR@ncrr.nih.gov

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Mutant Mouse Regional Resource Center at Harlan/University of Missouri

Harlan Sprague Dawley, Inc.
Laboratory Animal Medicine
298 S. Carroll Road
Indianapolis, IN 46229

Principal Investigator
Robert J. Russell, D.V.M.
317-894-7521; Fax: 317-894-4473 or 1840
E-mail: rjrusell@harlan.com

Additional Contacts, University of Missouri
John K. Critser, Ph.D.
800-669-0825; Fax: 573-884-7521
E-mail: critserj@missouri.edu

Lela K. Riley, Ph.D.
800-669-0825; Fax: 573-884-7521
E-mail: rileyk@missouri.edu

Current Research

The Harlan/University of Missouri node is focusing on two areas: Cryobiology research—Projects focus on improving methods for cryopreservation and banking of mouse spermatozoa and ovarian tissue. These research efforts are aimed at increasing the efficacy and efficiency of mouse genome banking. Health monitoring research—Projects focus on developing novel antemortem techniques for detection of microbial pathogens. These methods will be especially useful for monitoring mutant mouse colonies as they avoid the need to euthanize valuable mutant mice strictly for diagnostic evaluations.

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Mutant Mouse Regional Resource Center at Taconic Farms, Inc.

273 Hover Avenue
Germantown, NY 12526

Principal Investigator
James G. Geistfeld, D.V.M.
518-537-5200 x 227; Fax: 518-537-7287
E-mail: jgei@taconic.com

Additional Contact
Todd Little, Ph.D.
518-537-5200 x 237; Fax: 518-537-7287
E-mail: tlit@taconic.com

Current Research

The Taconic node is exploring the value of microarray technology for mutant phenotyping. A baseline of gene expression for "normal" mice is being established. This baseline will allow comparisons with mutant models. It is anticipated that this will allow identification of genetic perturbations associated with the mutation, thus allowing for translation of genotype into phenotype and function. In addition, behavioral phenotypic assays are being developed to screen for behavioral characteristics of mutant models and to identify modifier regions and genes that affect behavior. A whole-genome scan is also being performed on several strains commonly used to create mutants. This information will be used to plan accelerated backcrossing experiments.

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Mutant Mouse Regional Resource Center at University of California, Davis

Center for Comparative Medicine
One Shields Avenue
Davis, CA 95616

Principal Investigator
Stephen W. Barthold, D.V.M., Ph.D.
530-752-7913 or 754-9734; Fax: 530-752-7914
E-mail: swbarthold@ucdavis.edu

Additional Contact
Kent Lloyd, Ph.D.
530-752-7913; Fax: 530-752-7914
E-mail: kclloyd@ucdavis.edu

Current Research

The node at the University of California, Davis has developed a research tool called "The Visible Mouse." This Internet-accessible (ccm@ucdavis.edu/tvmouse) resource is an educational tool that provides anatomy, histology, and imaging modalities of the normal mouse, with navigational tools that allow the user to have access to the full depth and detail desired.

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Mutant Mouse Regional Resource Center at University of North Carolina

Program in Molecular Biology and Biotechnology
221 Fordham Hall, CB 3280
Chapel Hill, NC 27599-3280

Principal Investigator
Terry A. Van Dyke, Ph.D.
919-962-2145 or 4449; Fax: 919-962-4296
E-mail: tvdlab@med.unc.edu

Additional Contact
Virginia Godfrey, D.V.M., Ph.D.
919-966-2903; Fax: 919-962-4296
E-mail: virginia.godfrey@pathology.unc.edu

Current Research

The primary objective of the University of North Carolina node is to offer efficient distribution of breeder pairs for mutant mouse strains to interested investigators. The node imports, re-derives, genotypes, maintains and distributes new mouse strains. It cryopreserves new and existing mutant strains for archiving and for distribution. The node also phenotypically characterizes mouse strains with regard to histopathological, physiological, cell biological and molecular abnormalities. Research in mouse models is particularly strong, with major strengths in the areas of development and genomics, cardiovascular, and cancer research. Another major objective is to develop the ability to efficiently clone mice from somatic cells. This node is also developing reporter mouse strains that facilitate rapid phenotyping within particular cell/tissue types.

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Mutant Mouse Informatics Coordinating Center at The Jackson Laboratory

600 Main Street
Bar Harbor, ME 04609-1500

URL: www.mmrrc.org

Principal Investigator
Larry E. Mobraaten, Ph.D.
207-288-6373; Fax: 207-288-6149
E-mail: lem@jax.org

Additional Contact
Muriel T. Davisson, Ph.D.
207-288-6223; Fax: 207-288-6149
E-mail: mtd@jax.org

Current Research

The Informatics Coordinating Center (ICC) at The Jackson Laboratory provides an electronic network linking the MMRRCs by maintaining the database of the resources. The ICC database is updated continuously and includes live mouse and cryopreserved germplasm inventory from each MMRRC node.

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Cryopreservation of Murine Germplasm

The Jackson Laboratory
600 Main Street
Bar Harbor, ME 04609-1500

URL: www.jax.org

Principal Investigator and Contact
Larry E. Mobraaten, Ph.D.
207-288-6373; Fax: 207-288-6005
E-mail: lem@jax.org

Additional Contacts
Jackson Laboratory Animal Resources
800-422-MICE or 207-288-5845; Fax: 207-288-6150

Carlisle P. Landel, Ph.D.
207-288-6154; Fax: 207-288-6005
E-mail: clandel@jax.org

Research Emphasis/Objectives

To assure the safe preservation of scientifically valuable strains of laboratory mice by establishing a bank of frozen mouse embryos and sperm. The program staff is freezing and storing in liquid nitrogen embryos and sperm from selected strains of the more than 2,300 inbred and mutant strains of mice maintained at The Jackson Laboratory. Other objectives are to reduce the necessary number of different stocks or size of colonies maintained by conventional breeding procedures and to retard genetic drift.

Current Research

Cryopreservation of mouse embryos and spermatozoa.

Resources Provided

Reference Services

The repository contains frozen eight-cell mouse embryos and sperm from genetically defined strains of laboratory mice that are maintained at The Jackson Laboratory. Embryos and sperm from more than 2,000 different strains are preserved. Breeding pairs of mice are made available when such mice cannot be obtained from conventional breeding sources.

Index Terms

Cryopreservation, germplasm, mouse embryo, spermatozoa.

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Induced Mutant Resource

The Jackson Laboratory
600 Main Street
Bar Harbor, ME 04609-1500

URL: www.jax.org

Principal Investigator
Muriel T. Davison, Ph.D.
207-288-6223; Fax: 207-288-6149
E-mail: mtd@jax.org

Additional Contacts
Ray Vonder Haar, Ph.D.
207-288-6590
E-mail: rvh@jax.org

Stephen Rockwood
207-288-6437
E-mail: sfr@jax.org

Research Emphasis/Objectives

Research is being conducted on improved methods for assisted reproduction and speed congenic production. Most of the targeted mutants arrive on a mixed 129xC57BL/6 genetic background, and as many of these as possible are backcrossed onto an inbred strain (usually C57BL/6J). In addition, new mouse models are being created by intercrossing carriers of specific transgenes and/or targeted mutations. Simple sequence length polymorphism (SSLP) DNA markers are being used to characterize and evaluate differences between inbred strains, substrains, and embryonic stem cell lines.

Resources Provided

The Induced Mutant Resource (IMR) at The Jackson Laboratory was established in September 1992 in response to concerns from the scientific community regarding the cost, health, and distribution of genetically engineered mice (transgenic, targeted mutant, retroviral insertional mutant, and chemically induced mutant mice). The function of the IMR is to select, import, cryopreserve, maintain, and distribute these important strains of mice to the research community. To improve their value for research, the IMR also undertakes genetic development of stocks, such as transferring mutant genes or transgenes to defined genetic backgrounds and combining transgenes and/or targeted mutations to create new mouse models for research. Over 800 mutant stocks have been accepted by the IMR from 1992 through February 2000. Current holdings include models for research on cancer, breast cancer, immunological and inflammatory diseases, neurological diseases and behavioral, cardiovascular and heart diseases, developmental, metabolic and other diseases, reporter (e.g. GFP) and recombinase (e.g. cre/loxP) strains. About 8 strains a month are being added to the IMR holdings. A list of all strains may be obtained from the IMR Web site: www.jax.org/resources/documents/imr/. Online submission forms are available at www.jax.org/resources/documents/imr/. All mice can be ordered by calling The Jackson Laboratory's Customer Service Department at 1-800-422-MICE or 207-288-5845 or by faxing 207-288-6150. An online, searchable catalog and online order forms may be found at <http://jaxmice.jax.org/index.shtml>. A fee for mice is charged to partially recover strain maintenance costs and shipping expenses. For more information about the resource, contact any of the three investigators listed above or The Jackson Laboratory's Technical Information Service at micetech@jax.org. Updates on strain availability and other information are accessible by Internet at www.jax.org/resources/documents/imr/ or at <http://jaxmice.jax.org/index.shtml>.

Index Terms

Cryopreservation, disease models, mouse embryo, mouse models, mouse sperm, targeted mutations, transgenic mice.

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Mouse Mutant Gene Resource

The Jackson Laboratory
600 Main Street
Bar Harbor, ME 04609-1500

URL: www.jax.org

Principal Investigator and Contact
Muriel T. Davison, Ph.D.
207-288-6223; Fax: 207-288-6149
E-mail: mtd@jax.org

Additional Contacts
Kenneth R. Johnson, Ph.D.
207-288-6228
E-mail: krj@jax.org

Leah Rae Donahue, Ph.D.
207-288-6235
E-mail: lrd@jax.org

Eva M. Eichler, Ph.D.
207-288-6474
E-mail: eme@jax.org

Research Emphasis/Objectives

To discover and characterize new mouse models of human inherited conditions; to maintain as breeding pairs and preserve as frozen embryos new and established mouse mutations and chromosomal aberrations; to develop genetically suitable stocks of new and established mouse mutations for use in biomedical research; and to make these mutant stocks available to interested investigators in the scientific community.

Resources Provided

This resource encourages collaborations with visiting investigators to screen mutant and wild-derived strains for specific conditions, symptoms, biochemical or physiological defects, behavior, or other phenotypes of interest. The resource provides technical support for users of JAX mice to answer questions regarding genetics, husbandry, and characteristics of mutant mice. All mice can be ordered by calling The Jackson Laboratory's Customer Service Department at 1-800-422-MICE or 207-288-5845 or by faxing 207-288-6150. An online, searchable catalog and online order forms may be found at <http://jaxmice.jax.org/index.html>. A fee for mice is charged to partially recover strain maintenance costs and shipping expenses. For more information about the resource, contact any of the four investigators listed above. Updates on strain availability and other information are accessible by Internet at: www.jax.org/resources/documents/mmhome.html

The online form for submission of strains is available at www.jax.org/resources/documents/qrc/qrcspontout.html.

Mice

This resource develops and maintains strains of mice with specific mutant genes in various categories, including growth and development, reproduction, neurological, neuromuscular, vision and hearing, skeletal, immunological, skin and hair, pigmentation, kidney, and enzyme deficiencies. It also maintains stocks of mice with chromosomal aberrations including inversions, translocations, monosomy, and trisomy. In addition, several wild-derived inbred strains are maintained for linkage crosses. Details of the mouse strains available from The Jackson Laboratory are accessible by Internet at <http://jaxmice.jax.org/index.shtml>.

Index Terms

Genetic diseases, genetics, mouse, mouse models, mutations.

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Special Mouse Strains Resource

The Jackson Laboratory
600 Main Street
Bar Harbor, ME 04609-1500

URL: www.jax.org

Principal Investigator and Contact
Muriel T. Davisson, Ph.D.
207-288-6223; Fax: 207-288-6149
E-mail: mtd@jax.org

Additional Contacts
Leah Rae Donahue, Ph.D.
207-288-6235
E-mail: lrd@jax.org

Research Emphasis/Objectives

To make available to the biomedical research community a collection of special mouse strains for use in gene mapping, including genetic analysis of complex traits; to enhance the value of these strains by (1) increasing the number of DNA (microsatellite and SSLP) markers for which the recombinant inbred (RI) strain sets have been characterized to increase the utility of these strains in genetic mapping; (2) defining more precisely the extent of differential segments in the congenic strains to enhance their value as genetic mapping tools; and (3) phenotyping the chromosome substitution strains (CSS) strains to improve their baseline characterization, to develop a database of phenotypic information for the RI, CS and congenic strains in the resource, to develop graphic maps depicting the limits of the differential segments in the congenic strains.

Resources Provided

The Special Mouse Strains Resource (SMSR) maintains, cryopreserves and distributes mice from a group of special strains that are valuable tools for complex trait analysis and whose use will improve the efficiency of identifying genes in mouse models of multigenic human diseases.

Mice

The SMSR includes six RI strain panels, a number of congenic (CG) strains, and a set of 21 CSS developed by Dr. Joseph Nadeau at Case Western Reserve University. The RI strains include: 15 AXB (from an initial cross of an A/J female by a C57BL/6J male) and 14 reciprocal BXA, 34 BXD (C57BL/6J x DBA/2J), 12 BXH (C57BL/6J x C3H/HeJ), 13 CXB (BALB/cBy x C57BL/6By), and 14 SWXJ (SWR/J x SJL/Bm) strains. Each of Dr. Nadeau's CSS carries a single chromosome (1-19, X or Y) from strain A/J on an otherwise C57BL/6J background. CG strains maintained by the SMSR include 15 strains congenic for major histocompatibility complex (H2) haplotypes, 4 congenic at other immunology-related loci, 8 congenic for obesity-associated quantitative trait loci (QTL) and 8 for various other loci. These mice can be ordered by calling The Jackson Laboratory's Customer Service Department at 1-800-422-MICE or 207-288-5845 or by faxing 207-288-6150. An online, searchable catalog and online order forms may be found at:

<http://jaxmice.jax.org/index.html>. A fee for mice is charged to partially recover strain maintenance costs and shipping expenses. For more information about the resource, contact either of the investigators listed above. Updates on strain availability and other information also are accessible by Internet at: <http://jaxmice.jax.org/index.html>.

Index Terms

Complex trait analysis, consomic, gene mapping, genetic diseases, genetics, mouse, mouse models, mutations, quantitative trait loci, quantitative trait loci, recombinant inbred.

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Peromyscus Genetic Stock Center

University of South Carolina
Department of Biological Sciences
700 Sumter Street Columbia, SC 29208

URL: <http://stkctr.biol.sc.edu>

Principal Investigator
Michael J. Dewey, Ph.D.
803-777-4132; Fax: 803-576-5780
E-mail: dewey@biol.sc.edu

Copincipal Investigator
Wallace D. Dawson, Ph.D.
803-777-3107; Fax: 803-576-5780
E-mail: wdawson@stkctr.biol.sc.edu

Contact and Colony Manager
Janet Crossland
803-777-3107; Fax: 803-576-5780
E-mail: crosslan@stkctr.biol.sc.edu

Research Emphasis/Objectives

Development of cryopreservation techniques that are applicable to *Peromyscus* sperm to enable long-term preservation of mutant stocks.

The mechanism and genetics of hybrid dysgenesis in reciprocal hybrids of *P. maniculatus* and *P. polionotus*. Offspring of matings in one direction are markedly oversized; the reciprocal cross produces undersized offspring.

Development of an intermediate density map utilizing PCR-based type 1 (functional genes) and type II (microsatellite) markers as well as single gene mutants with coat color or neurological phenotypes; and interspecific crosses between *P. maniculatus* and *P. polionotus* as well as whole genome radiation hybrids for linkage determinations. Fruition of the mapping project will benefit a wide range of investigators interested in using *Peromyscus* to study the genetic basis of speciation, genome imprinting, disease vector biology, and behavioral and physiological adaptation to habitat.

Resources Provided

The *Peromyscus* Genetic Stock Center was established in 1985 and functions to provide a reliable source of genetically defined and virus-free animals and related materials to the scientific and educational communities. The center currently keeps nine species and more than 27 distinctive mutant and other genetically defined stocks. Included among the species maintained are *P. californicus*, *P. leucopus*, *P. eremicus*, *P. aztecus*, *P. melanophrys* as well as two subspecies each of *P. maniculatus* and *P. polionotus* and three inbred lines of *P. leucopus*. Among the mutant stocks are 17 with altered coat phenotypes, 3 with neurological symptoms, and 6 others with developmental/physiological effects. One of these is a line deficient in alcohol dehydrogenase that has been widely used in studies of alcohol metabolism. The stock center also supplies biological materials including fresh, frozen and preserved tissues, molecular probes and libraries. The center functions as a clearinghouse for information regarding this genus by sponsoring an Internet database (PeroBase: <http://votan.cs.sc.edu/perobase>), and the semi-annual *Peromyscus Newsletter*. The center maintains a collection of over 3,000 *Peromyscus*-related reprints of published articles, books and journals, photocopies of which are available upon request.

Index Terms

Cryopreservation, deer mouse, hantavirus, Lyme disease, monogamy, mouse genetics, *Peromyscus*, white-footed mouse.

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Rat Resource and Research Center

University of Missouri
Comparative Medicine Center and Research Animal
Diagnostic and Investigative Laboratory
Columbia, Missouri 65211

Principal Investigator and Contact
John K. Critser, Ph.D.
573-884-9469; Fax: 573-884-7521
E-mail: critserj@missouri.edu

URL: www.radil.missouri.edu/rrrc

The Rat Resource and Research Center (RRRC) was established in 2001. The RRRC is a multi-institutional consortium of investigators including John K. Critser, Ph.D., and Lela K. Riley, Ph.D., at the University of Missouri; Robert J. Russell, D.V.M., at Harlan Sprague Dawley, Inc.; and Philip M. Iannaccone, M.D., Ph.D., at Northwestern University Children's Memorial Institute for Education and Research.

Research Emphasis/Objectives

Research projects are focused in three major areas of importance to rats as animal models: Development of efficacious methods for nuclear transfer in the rat; development of efficient methods for genome resource banking and strain/stock reconstitution, including ovarian tissue preservation and transplantation in combination with artificial insemination with cryopreserved spermatozoa; and improved methods for health monitoring of rats using molecular diagnostics and environmental monitoring.

Resources Provided

The overall goal is to establish a center for distributing high quality, well-characterized inbred, hybrid and mutant rats to investigators. To this end, the RRRC will select and import rat strains and stocks important to the biomedical research community; rederive rats to a pathogen-free state; cryopreserve gametes and embryos; perform genotyping, phenotyping and infectious disease monitoring to assure the quality of the rats, and distribute rats to investigators as live rats, cryopreserved germplasm or tissues.

Index Terms

Animal models, cryopreservation, genotyping, health monitoring, nuclear transfer, phenotyping, rats, reproductive biology.

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Transgenic Mice With Altered Calcium Handling

Pharmacology and Cell Biophysics
University of Cincinnati College of Medicine
231 Albert Sabin Way
P.O. Box 670575
Cincinnati, OH 45267-0575

Principal Investigator and Contact
Evangelia G. Kranias, Ph.D.
513-558-2377; Fax: 513-558-2269
E-mail: litisa.kranias@uc.edu

URL: www.med.uc.edu/p40resource/

Research Emphasis/Objectives

The recent development of phospholamban knockout and phospholamban overexpression mice has revealed that phospholamban is a major regulator of basal contractility in the mammalian cardiac, smooth, and skeletal muscles. The regulatory effects of phospholamban are mediated through the Ca^{2+} -ATPase in sarcoplasmic reticulum (SERCA2), the key enzyme involved in muscle relaxation. Dephosphorylated phospholamban is an inhibitor of the sarcoplasmic reticulum Ca^{2+} -ATPase activity, and phospholamban relieves this inhibition. The overall research hypothesis is that alterations in the levels of the sarcoplasmic reticulum Ca^{2+} -ATPase or phospholamban, and the phosphorylated states of phospholamban are associated with alterations in calcium homeostasis and function of the muscles. Thus, the long-range research goal of this resource is to generate animal models with altered expression in each of these two key Ca^{2+} -cycling proteins; and altered expression of phospholamban phosphorylation mutants in cardiac, smooth, and slow-twitch skeletal muscle. These mouse models will be made available to the biomedical community at large to carry out further in-depth studies and to elucidate the mechanisms underlying intracellular calcium regulation and physiological responses in health and disease.

Resources Provided

This resource generates and maintains mouse models with genetic alterations in either phospholamban or the sarcoplasmic reticulum Ca^{2+} -ATPase in cardiac, smooth, or slow-twitch skeletal muscle. These models are initially characterized in the resource and then they are made available to interested investigators in the scientific community. A list of all current models may be obtained from the Sarcoplasmic Reticulum Mutant Mouse Resource (SR-MMR) Web site.

Index Terms

Ca^{2+} -ATPase, calcium, genetics, knockout mouse, muscle, phospholamban, sarcoplasmic reticulum, transgenic

mice.

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National Center for Research Resources (NCRR)
National Institutes of Health
One Democracy Plaza, 9th Floor
6701 Democracy Boulevard, MSC 4874
Bethesda, MD 20892-4874



National Institutes of Health (NIH)
Bethesda, Maryland 20892



Department of Health
and Human Services

